

Varicocele

By

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Definition of varicocele

Varicocele means abnormal dilatation of the pampiniform plexus of veins of the testis which represents the veins of the spermatic cord. The name being derived from its resemblance to a vein (pampinustendril) .

Historical background

Varicocele and its association with infertility has been recognized for centuries. *Celsus*, in the first century (AD) described dilatation of the scrotal veins and noted an association between varicocele and testicular atrophy.

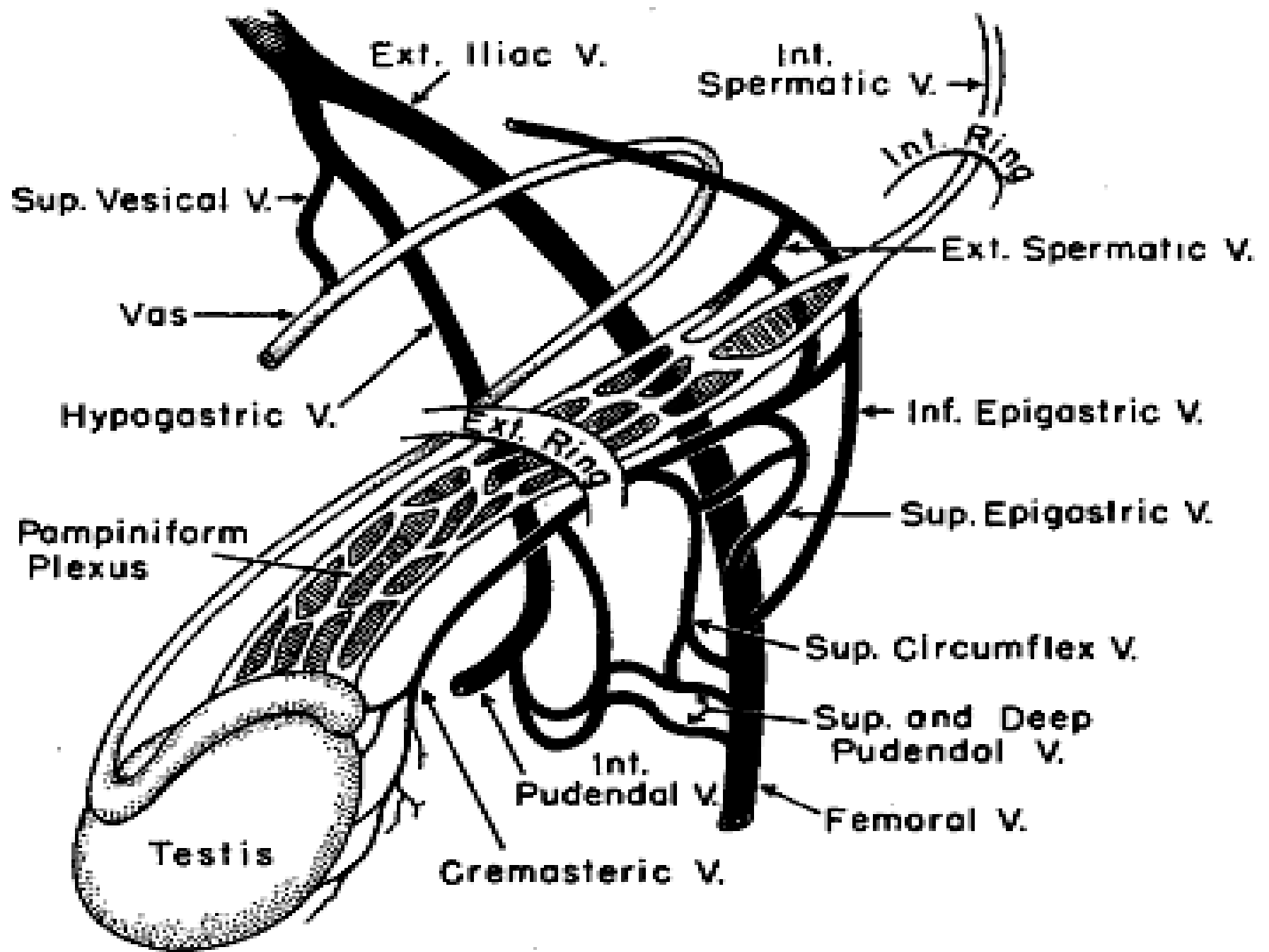
In 1929, *Macomber and Sanders* reported the relationship between varicocele repair improvement in semen parameter and fertility. Since then, causal relationship between the varicocele and impaired fertility has been assumed.

Incidence varicocele

- Varicocele occurs in the general population of males in 10% to 15% and presents in 30-50 % of males with primary infertility and in 80% of men with secondary infertility.
- More than 80% of varicoceles are not associated with infertility .
- As regards the incidence of varicocele in the relatives of varicocele patient it is 53% in the first-degree relatives of men with varicocele.
- Varicocele occurs more commonly as isolated left-sided lesions (60%-90%). but recent studies have shown bilaterality in 15%-57% of cases

Blood supply of the testis

- The arterial supply to the testis is derived from the testicular artery, with contributions from the vasal and cremasteric arteries.
- the venous drainage of the scrotal contents includes the testicular (internal spermatic) vein, which drains to the renal vein on the left or the vena cava on the right; the vasal (deferential) vein, which drains into the vesicular veins; and the cremasteric (external spermatic) vein, which drains into the inferior epigastric vein. These vessels are highly anastomotic and form the pampiniform plexus.



Etiology of varicocele

Varicocele is classified according to the etiology into:

1. **Primary varicocele.**
2. **Secondary varicocele.**

Primary varicocele

Varicocele formation may be due to:

- 1. *Position*** : varicoceles may be a consequence of man's upright posture, because they are rare in other species.
- 2. *Anatomical factors***: The long course of the internal spermatic vein is believed to result in increased hydrostatic pressure that is transmitted down the veins to the scrotal pampiniform plexus, causing dilation and tortuosity of these vessels. Collateral venous channels between right and left internal spermatic vein play an important role.
- 3. *Disorder of the valves***: absent or incompetent valves within the internal spermatic vein → reflux of venous blood into the pampiniform plexus.

Primary varicocele

4. *Nutcracker phenomena*: Proximal one that occurs when the testicular vein is compressed between the superior mesenteric artery and aorta and The distal one is due to compression of the left common iliac vein by pressure of the right common iliac artery.
5. *Increased arterial blood flow* : Which exceeds the venous capacity ~~ven~~ venous dilatation.
6. *Genetic factors*: a high rate of Y chromosome microdeletions in 17.5% in patients with left-sided varicocele.

Secondary varicocele

- Secondary varicocele occurs when the renal or internal spermatic vein is compressed by renal or retroperitoneal neoplasm . Secondary varicocele characteristically does not disappear when the patient attains the supine position

Histopathological changes with varicocele

- 1. Vascular changes:* include endothelial prominence, intimal fibrosis and an increased amount of collagen in the media in veins, venules, and capillaries.
- 2. Changes in the tunica vasculosa and albuginea:* Increase number of veins and arteries in the tunica vasculosa and the tunica albuginea was thick owing to the increased number of muscle fibers or their hypertrophy.

Histopathological changes with varicocele

3. *Interstitial changes* : Leydig cell abnormalities may be found, ranging from atrophy to hyperplasia.
4. *Tubular changes*: Include decreased spermatogenesis, maturation arrest, and tubular thickening. These findings are present in both testes and are more pronounced on the side ipsilateral to the varicocele. There is also decreased number of Sertoli cells per tubule and sloughing of the germinal epithelium.

Smoking and varicocele

- Smokers have been reported to have at least a twofold increased incidence of varicoceles. Furthermore, smokers with varicoceles have a tenfold increase in the incidence of oligospermia when compared with nonsmokers with varicoceles.
- This observation is theorized to be the result of a direct gonadotoxic effect of nicotine, a nicotine-induced catecholamine release from the adrenal medulla with retrograde flow to the testis, the presence of cadmium in cigarettes, or a free radical source contributing to oxidative damage.

Effects of varicocele on fertility

- It is quite clear that varicoceles are detrimental to testicular growth and spermatogenesis. However, the majority of men with varicoceles are fertile because the effect is modest or they started with a high spermatogenic potential.
- Varicoceles are the most common and easily corrected cause of male factor subfertility. Despite such findings, it is apparent that more than 85% of men with varicocele are fertile.

Pathophysiology of varicocele

Effects on fertility

Several mechanisms have been hypothesized to explain the testicular dysfunction that accompanies varicoceles:

- 1 Hyperthermia:*** This is the most widely accepted mechanism for the alteration of testicular function secondary to varicocele. Heat on the testis may can cause a direct effect on germ cells, leading to altered metabolism, apoptosis, altered Sertoli cell function, vascular changes with increased arteriovenous shunting, decreased activity of the enzymes involved in DNA synthesis, or a decreased delivery of nutrients and oxygen to the testis.

Pathophysiology of varicocele

Effects on fertility

- 2 Renal and adrenal metabolites:** Elevated levels of norepinephrine and prostaglandins E and F have been identified within the spermatic vein.
- 3 Hypoxia:** men with varicoceles had significantly elevated pressures → stagnation of blood & hypoxia.
- 4 Reactive oxygen species:** Uncontrolled and excessive reactive oxygen species production, as well as decreased antioxidant defenses, are thought to have a role in the infertility associated with varicocele. Excessive reactive oxygen species can cause cellular damage by means of lipid peroxidation, resulting in decreased sperm motility and viability, impaired capacitation and acrosome reaction, and decreased capacity for sperm–oocyte fusion.

Pathophysiology of varicocele

Effects on fertility

- 5 Gonadotoxins:** Gonadotoxins are implicated as a cofactor in the pathogenesis of varicocele.
- 6 Immunologic:** Sperm bound immunoglobins are present in a greater percentage of infertile men with varicocele.
- 7 Apoptosis:** Varicoceles are associated with an increase in apoptosis within testicular tissue .
- 8 Enzymatic function:** Topoisomerase I and DNA polymerase in testicular tissue have lower activity in cases with varicocele. The level of serum Transforming growth factor beta 1 was higher in varicoceles than in the normal testes.

Predisposing factors for predominance of left-sided varicocele:

- 1 The left internal spermatic vein drains at right angle into the left renal vein, taking a course that is approximately 8-10 cm longer than that of the right internal spermatic vein, which enters the inferior vena cava at an oblique angle .
- 2 On the right side, the adrenal, renal, and spermatic veins all drain directly into the inferior vena cava. This anatomy is in contrast to that on the left side, where the spermatic vein and adrenal veins all drain into the left renal vein, which has a relatively poorer drainage.

Predisposing factors for predominance of left-sided varicocele:

- 3 Absence of the venous valves is more commonly found on the left side than on the right.
- 4 The nutcracker phenomenon: refers to compression of the venous drainage system of the testis. This obstruction to flow is thought to result in the development of collateral drainage, increased venous pressure, and stasis.
- 5 Differences in the configuration of the right and left internal spermatic veins and their embryologic origins are thought to contribute to this marked left-sided predominance

Bilateral effects of varicocele

- The most prominent theories of contralateral effect of varicocele included: Increase testicular temperature, reflux of toxic metabolites through collateral venous circulation to the contralateral testis and modification of the normal hypothalamic pituitary gonadal axis.
- One co-factor is an elevation in left testicular cadmium (Cd^{2+}) levels, leading to alteration in calcium homeostasis that implicated in impaired spermatogenesis in left varicocele.

Effects of varicocele on testicular volume

- It is quite clear that varicoceles are detrimental to testicular growth and spermatogenesis. Varicoceles are associated with smaller ipsilateral testes. In addition Varicocele repair has been demonstrated to result in catch-up growth in adolescents with varicoceles and ipsilateral loss of testicular volume.

Effects of varicocele on semen parameters

- Semen parameters impairments in varicocele , most commonly, a decrease in motility (90%) and a sperm concentration less than 20×10^6 (65%). The common morphologic changes, referred to as a “stress pattern,” included increased numbers of amorphous cells, immature forms (usually early spermatids), and greater than 15% tapered forms.
- The most common anomaly of semen analysis is the decrease in the motility that may be associated with increase in the abnormal forms. In addition, sperm motility is the first parameter that improves after varicocelectomy.

Effects of varicocele on semen parameters

- *Varicocele and sperm function tests:* 97% of infertile men with varicocele scored <15% penetration in the zona-free assay compared with 61% of fertile men with varicocele and 68% of fertile men without varicocele.

Diagnosis of varicocele

1 History.

2 Clinical examination :

- **Subclinical** : Not palpable or visible either at rest or during Valsalva's (demonstrated by finding of reflux on Doppler examination).
- **Grade 1**: Palpable during Valsalva's maneuver but not otherwise.
- **Grade 2** : Palpable at rest but not visible .
- **Grade 3** : Visible and palpable at rest.

Diagnosis of varicocele

3 Investigations:

A- Doppler .

B-Duplex ultrasonography.

C-Venography.

D-Thermography and thermometry.

E-Scintigraphy.

F-(CT) Scan.

G-MRI .

H-Hormonal studies : including FSH,LH, Testosterone,
GnRH stimulation test, Inhibin B and Transferrin.

Treatment of varicocele

- The goal of varicocele treatment is to improve testicular function and seminal parameters and to increased pregnancy rates.
- It includes surgical and non surgical methods.

Treatment of varicocele

- *surgical methods:*

A-Inguinal approach.

B-Subinguinal approach.

C-Retroperitoneal approach.

D-Laparoscopic approach.

E-Scrotal approach.

Treatment of varicocele

- *Nonsurgical methods:*

1-Transvenous Occlusion (Embolization).

2-Medical treatment:

- a. **Cinnoxiam.**
- b. **Melatonin.**
- c. **Kallikrein.**

